CONCLUSIONS The age of onset of aortic dissection of female patients older than men, sudden chest pain symptoms women is obvious than men. while symptoms of irritable male more common. aortic intramural hematoma is more common in women. Suffering from acute type AAD women patients have higher operative mortality.

GW26-e4000

Kv4.3 Expression Improves Cardiac Contraction Without Inhibition of Relaxation in Heart Failure

Yanggan Wang
Zhongnan Hospital of Wuhan University

OBJECTIVES To test whether expression of Kv4.3 in HF ventricular myocytes would improve cardiac contraction without affecting relaxation by inhibition of membrane associated CaMKII.

METHODS HF was generated in mice by thoracic aortic binding and Kv4.3 was expressed in HF ventricular myocytes by left ventricular adenoviral injection with Ad-Kv4.3 (Ad-β-gal injection was used as control). $[Ca^{2+}]_i$ and sarcomere length were measured by IonOptix Ca^{2+} image system. Myofilament sensitivity to Ca^{2+} was assessed by measuring the gradient of cell length-fura2 trajectory during contraction and late relaxation.

RESULTS HF ventricular myocytes with Kv4.3 expression presented a significant increase in fractional shortening and Ca^{2+} transient with a reduction in diastolic SR Ca^{2+} leak, and a recovery of frequency-dependent acceleration of relaxation (FDAR), an intrinsic mechanism allowing faster ventricular relaxation and diastolic filling at fast heart rates. In contrast to KN93, a pharmacological CaMKII inhibitor, Kv4.3 expression did not affect myofilament sensitivity to Ca^{2+}, assessed by the changes of length-fura2 trajectory gradients. In line with this, a phospho-Ser-antibody showed that unlike KN93, which significantly reduced phosphorylation in the Tn-I that co-immunoprecipitated with CaMKII, Kv4.3 expression did not alter Tn-I phosphorylation. In vivo study showed that Kv4.3 expression increased EF from 45 ± 1% in HF mice transfected with Ad-β-gal (n=11) to 73 ± 2% in mice transfected with Ad-Kv4.3 (n=10, $p<0.05$), while the E/E' ratio was unchanged (39 ± 2 vs. 35 ± 2, $p>0.05$).

CONCLUSIONS Our results suggest that Kv4.3 expression improves myocardial contraction without detrimental effect on cardiac relaxation. Instead, it recovers FDAR.

GW26-e4022

SRY Gene Transferred by Extracellular Vesicles Accelerates Atherosclerosis by Promotion of Leukocyte Adherence to Endothelial Cells

Jin Cai, Chunyu Zeng
Department of Cardiology, Daping Hospital, The Third Military Medical University, Chongqing, China

OBJECTIVES Extracellular vesicles (EVs) participate in important biological processes, including horizontal transfer of borne molecules among neighboring cells. Our previous study showed the existence of DNA in EVs that have the ability to influence the function of recipient cells by increasing DNA-coding mRNA and protein levels. SRY (sex determining region, Y), a gene in the Y chromosome responsible for increasing expression of angiotensin II and noradrenaline, is associated with risk of coronary artery disease (CAD) in men. We hypothesize that SRY DNAs in plasma EVs is involved in the pathogenesis of atherosclerosis by the transfer of SRY DNA to recipient cells, e.g., leukocytes and endothelial cells, and increased adherence of leukocytes to endothelial cells.

We set out to investigate whether and how SRY (sex determining region, Y) DNAs in plasma extracellular vesicle (EVs) is involved in the pathogenesis of atherosclerosis.

METHODS PCR and gene sequencing found SRY gene fragment in plasma EVs from male but not from female patients; EVs from male patients with coronary artery disease (CAD) had higher SRY gene copy number (GCN) than healthy subjects.

RESULTS Additional studies found that leukocytes, the major source of plasma EVs, had higher SRY GCN and mRNA and protein expression in male CAD patients than controls. After incubation with EVs from SRY-transfected HEK293 cells, monocytes (THP-1) and endothelial cells (HUVECs), which do not endogenously express SRY protein, were found to express newly-synthesized SRY protein. This resulted in an increase in adherence factors, CD11-a in THP-1 cells and ICAM-1 in HUVECs. Electrophoretic mobility shift assay showed that SRY protein increased the promoter activity of CD11-a in THP-1 cells and ICAM-1 in HUVECs. There was an increase in THP-1 cells adherent to HUVECs after incubation with SRY-EVs. SRY DNAs transferred from EVs have pathophysiological significance in vivo; injection of SRY EVs to ApoE-/- mice accelerated atherosclerosis.

CONCLUSIONS The SRY gene in plasma EVs transferred to vascular endothelial cells may play an important role in the pathogenesis of atherosclerosis; this mechanism provides a new approach to the understanding of inheritable CAD in men.

GW26-e1814

Role of Monocyte/Macrophage in TRPV1 Ablation-Induced Renal Injury in Salt-Sensitive Hypertension

Youping Wang, Mingjun Zhu, Leilei Fan, Miaomiao Fan, Lin Cui, Xiaoxiao Wang, Shiyang Xie, Si Shen
Central Laboratory and Division of Cardiology, First Affiliated Hospital, Henan University of Traditional Chinese Medicine, Zhengzhou, 450000, China

OBJECTIVES Our studies show that deletion of the transient receptor potential vanilloid type 1 (TRPV1) gene aggravates deoxycorticosterone acetate (DOCA)-salt hypertension-induced renal injury, which is associated with increased renal monocyte chemoattractant protein-1 (MCP-1) production and monocyte/macrophage infiltration. The results suggest that TRPV1 ablation-induced aggravation of renal injury in DOCA-salt hypertension may be the result of enhanced renal monocyte/macrophage infiltration that is dependent of the MCP-1/C-C chemokine receptor 2 (CCR2) signaling pathway. Therefore, we hypothesized that MCP-1/CCR2-mediated monocyte/macrophage infiltration is a critical determinant of TRPV1 ablation-induced renal injury in salt-sensitive hypertension.

METHODS We induced salt-sensitive hypertension for 4 weeks by uninephrectomy and DOCA-salt in wild type (WT) and TRPV1-null mutant ($TRPV1^{-/-}$) mice with or without RS504393, a selective CCR2 antagonist.

RESULTS DOCA-salt treatment increased systolic blood pressure (SBP) to the same degree in both strains, but increased urinary excretion of albumin and 8-isoprostane and decreased creatinine clearance with greater magnitude in $TRPV1^{-/-}$mice compared to WT mice (89.3±5.2 vs. 26.5±3.4 μg/24h; 4.24±0.45 vs. 1.52±0.21 ng/24h; 98±19 vs. 168±14 ml/24h, $P<0.05$). DOCA-salt treatment also caused renal glomerulosclerosis, tubulointerstitial injury, collagen deposition, monocyte/macrophage infiltration, proinflammatory cytokine and chemokine production, and NF-κB activation in greater degree in $TRPV1^{-/-}$ mice compared to WT mice (glomerulosclerosis index: 0.78±0.15 vs. 0.35±0.14; tubulointerstitial injury score: 3.37±1.0 vs. 2.01±0.49; collagen content: 21.8±2.3 vs. 13.8±2.4 μg/mg dry tissue; monocyte/macrophage infiltration: 74±4 vs. 42±5 cells/mm^2; TNF-α: 1.03±0.22 vs. 0.76±0.21 pg/mg protein; MCP-1: 10.35±1.19 vs. 6.00±0.86 pg/mg protein; p65-NF-κB protein: 54±5 vs. 36±3 ng/mg protein, $P<0.05$). Blockade of the CCR2 with RS504393 (4 mg/kg) had no effect on SBP in DOCA-salt-treated WT or $TRPV1^{-/-}$ mice compared to their respective controls. However, treatment with RS504393 ameliorated renal dysfunction and morphological damage, and prevented the increase in monocyte/macrophage infiltration, cytokine/chemokine production, and NF-κB activity in both DOCA-salt hypertensive strains with a greater effect in DOCA-salt-treated $TRPV1^{-/-}$ compared to DOCA-salt-treated WT mice.

CONCLUSIONS Our data showed that blockade of CCR2 with RS504393 attenuated DOCA-salt hypertension-induced renal injury in WT and $TRPV1^{-/-}$ mice independently of their effects on blood pressure. The protective effect was greater in $TRPV1^{-/-}$ mice compared to WT mice. The results suggest that deletion of TRPV1 aggravated salt-sensitive hypertension-induced renal damage possibly via enhancement of the MCP-1/CCR2-mediated monocyte/macrophage infiltration. [This work was supported by a grant from the National Natural Science Foundation of China (No. 81170243)].

GW26-e0197

Exploring the Active Ingredients in Chinese Yellow Wine Which Could Inhibit the Progress of Atherosclerosis in LDLR Knockout Mice

Liping Meng,[1,2] Xiaoya Zhai,[2] Chenjian Jiang,[2] Zheng Ji,[2] Yan Guo,[2] Jufang Chi,[2] Hangyuan Guo[1,2]
[1]Shaoxing People's Hospital; [2]The First Clinical Medical College of Wenzhou Medical University

OBJECTIVES To explore the active ingredients in Chinese yellow wine which could inhibit the progress of atherosclerosis in LDLR knockout mice.

METHODS Six weeks old LDLR-/- male mice (n=56) were randomly allocated into 7 groups (8 mice in each group): normal control group (NC), high fat group (HF), high fat and yellow wine oligosaccharides modulation group (HFYWO), High fat and yellow wine polypeptides modulation group (HFYWPP), high fat and yellow wine polyphenols modulation group (HFYWP), high fat and alcohol modulation group (HFA), high fat and yellow wine modulation group (HFYW). After 16 weeks intervention, mice were sacrificed. The levels of serum lipids were examined. The morphological changes of aorta artery were observed under microscope. The expressions of matrix metalloproteinase 2 (MMP-2), matrix metalloproteinase 9 (MMP-9), tissue inhibitor of metalloproteinase2 (TIMP-2) were determined by Western blot. The activations of MMP-2, MMP-9 were determined by Gelatin Zymography.

RESULTS Compared to NC, high fat diet could rise the serum lipid level, improve the atherosclerosis lesion area and increase the expression and activation of MMP-2 and MMP-9. Compared with HF, the level of LDL-C, TG and TC in the serum of mice were decreased in HFYWP, HFYWPP and HFYW, $P<0.05$. The atherosclerosis lesion area in HFYWPP (10.1±1.23), HFYWP (7.3±0.86) and HFYW (5.1±0.34) were significantly smaller Compared with HF (15.3±1.84), $P<0.05$. Yellow wine polypeptides, polyphenols and Chinese yellow wine could inhibit the expression and activation of MMP-2 and MMP-9 compared with HF, $P<0.05$. There is no significant difference between each group on the expression of TIMP-2.

CONCLUSIONS Polypeptides and polyphenols in the Chinese yellow wine could inhibit the high fat diet induced progression of atherosclerosis in LDLR-/- mice, the mechanisms may be that these ingredients in the yellow wine could regulate blood lipid and keep the balance between MMPs and TIMPs.

GW26-e0375

Effects of Yellow Wine on Rat Vascular Endothelial Cells Induced by TNF-α

Fei Zhao, Liping Meng, Yan Guo, Hangyuan Guo
Department of Cardiology, Shaoxing People's Hospital, Shaoxing Hospital of Zhejiang University

OBJECTIVES To determine similarities in effect of yellow wine as compared statin and the possibility that yellow wine on rat vascular endothelial cells induced by TNF-α.

METHODS Isolation, cultivation, purification and identification of vascular endothelial cells of rat thoracic aorta in vitro were conducted. The passages 3 of VECs were used in all studies. The viability of VECs was determined and the optimal concentration of the wine was selected using MTT method. Then we divided cells into 9 groups: control, TNF-α, TNF-α+ rosuvastatin (10 umol/L), TNF-α+ethanol 0.5%, TNF-α+yellow wine 0.5%, TNF-α+ethanol 1.0%, TNF-α+yellow wine 1.0%, TNF-α+ethanol 1.5%, and TNF-α+yellow wine 1.5% and the cells were given the corresponding treatment. NO production of culture supernatant was determined by nitrate reduction method and eNOS activity of cells was measured by chemical colorimetric method after the corresponding treatment for 24 h. The expression of eNOS, iNOS, and ICAM-1 protein were detected by western blotting after the corresponding treatment for 48 h.

RESULTS

1. Compared with control group, the NO production in TNF-α group was decreased significantly (P<0.05). Compared with TNF-α group, the rosuvastatin, yellow wine 1.0% and yellow wine 1.5% groups can increase NO production (P<0.01 or P<0.05). The effect in ethanol 0.5%, 1.0%, 1.5% and yellow wine 0.5% groups was not significant.
2. Compared with control group, eNOS activity in TNF-α group was significantly decreased (P<0.05). Compared with TNF-α group, eNOS activity in rosuvastatin, yellow wine 1.0% and yellow wine 1.5% groups were significantly increased (P<0.01 or P<0.05). However, there was no significant difference among ethanol 0.5%, 1.0%, 1.5% and yellow wine 0.5% groups.
3. Compared with the TNF-α group, eNOS protein expression in the rosuvastatin, and yellow wine 1.0%, and 1.5% groups were significantly increased (P<0.01). Protein expression of iNOS and ICAM-1 in the rosuvastatin, yellow wine 1.0%, and 1.5% groups were significantly decreased (P<0.01). Compared with the rosuvastatin group, eNOS, iNOS, and ICAM-1 protein expression in the yellow wine (0.5% -1.5%) groups were significantly different (P<0.01 or P<0.05).

CONCLUSIONS

1. TNF-α can reduce NO production of culture supernatant in VECs, inhibit the eNOS activity and the expression of eNOS protein, and enhance the expression of iNOS and ICAM-1 protein. It promotes the development of atherosclerosis by causing endothelial dysfunction.
2. Yellow wine and rosuvastatin can improve vascular endothelial function by increasing NO production of culture supernatant, enhancing eNOS activity and expression of eNOS protein and inhibiting iNOS and ICAM-1 protein levels.
3. Yellow wine is similar to the role of rosuvastatin.
4. The result suggests that yellow wine might affect the development of atherosclerosis through this mechanism and contribute to its beneficial effects on the cardiovascular system.

GW26-e0687

The Endoplasmic Reticulum Stress Signaling Pathways in Protection of Myocardium Ischemia/Reperfusion Injury Model Rats by Pioglitazone

Huanzhen Chen,[1] Xiangli Cui,[2] Xiuping Jiang,[1] Yan Li,[1] Wenyan Ma[1]
[1]The First Hospital of Shanxi Medical University; [2]Shanxi Medical University

OBJECTIVES To observe influence of Pioglitazone on the changes of expression of GRP78 JNK/ p-JNK and caspase-12 in Ischemia reperfusion in rats, and discuss the myocardial protective effect of pioglitazone to the endoplasmic reticulum stress way through the JNK pathway.

METHODS Forty male rats were randomly divided into four groups: sham operation group (n=10), ischemia-reperfusion group (n=10), pioglitazone 10 mg treated group (n=10), pioglitazone 10 mg treated and using SP600125 group (n=10). Left anterior descending coronary artery was ligated for 30 min and reperfused for 2 hour to establish the model of ischemia-reperfusion. The number of myocardial apoptotic cells were detected by TUNEL staining, the expression of GRP78 and caspase-12 protein were detected by immunohistochemical staining. Western blot was performed to detect the expression of JNK and p-JNK.

RESULTS

1. **Myocardial cell apoptosis index** myocardial cell apoptosis index in ischemia reperfusion group is (35.98±2.6%), sham operation group (1.87±0.13) %, pioglitazone group (23.70±1.08) %, pioglitazone combined SP600125 group (19.16±0.44)%. Pioglitazone group AI was lower compared to the ischemia reperfusion group ($P < 0.05$), but higher than that of the sham operation group ($P < 0.05$). Though the pioglitazone combined SP600125 group AI is higher than that of ischemia reperfusion group, the difference was not statistically significant ($P = 0.05$).
2. **2 GRP78 protein average integral optical density AIOD** AIOD in ischemia-reperfusion group is 0.437±0.166, in sham operation group is 0.027±0.045,in pioglitazone group is 0.400±0.107,in pioglitazone combined SP60025 group is 0.385±0.237. The expression of GRP78 in pioglitazone group and Pioglitazone combined SP60025 group were lower than in ischemia reperfusion group ($P < 0.05$), but higher than that of the sham operation group ($P < 0.05$).
3. **Caspase-12protein average integral optical density** For AIOD, ischemia-reperfusion group is 1.321±0.081, sham operation group is 0.173±0.070, pioglitazone group is 0.746±0.076, pioglitazone combined SP60025 group is 0.514±0.059, the expression of GRP78 in pioglitazone group and Pioglitazone combined SP60025 group were lower than in ischemia reperfusion group ($P < 0.05$), but higher than that of the sham operation group ($P < 0.05$).
4. **JNK, p-JNK protein expression** Compared with the sham group JNK protein expression did not change significantly, but its activated form p-JNK expression changes significantly, compared with the sham group p-JNK expression of I/R group increased 3.46 -fold ($P < 0.05$), compared with I/R group p-JNK of pio group downregulated 1.22 -fold ($P < 0.05$), compared with pio group p-JNK of pioglitazone combined SP600125 downregulated 0.78 -fold ($P < 0.05$)

CONCLUSIONS Ischemia-reperfusion can activate JNK access and induce severe ER then aggravate cell apoptosis induced by ERS. Pioglitazone could reduce cell apoptosis induced by ERS, which are important protection factors, are mediated by JNK.

GW26-e0721

Macrophage Migration Inhibitory Factor (MIF) Promotes the Expression of GLUT4 Glucose Transporter Through MEF2 and Zac1 in Cardiomyocytes

Zhixin Shan, Shulin Wu
Guangdong General Hospital, Guangdong Cardiovascular Institute

OBJECTIVES Evidence shows that both macrophage migration inhibitory factor (MIF) and GLUT4 glucose transporter are involved in